

(3) The Commissioner will evaluate all comments received. If he concludes that there is a lack of convincing evidence that the substance is GRAS or is otherwise exempt from the definition of a food additive in section 201(s) of the Act, he will publish a notice thereof in the FEDERAL REGISTER. If he concludes that there is convincing evidence that the substance is GRAS, he will publish an order in the FEDERAL REGISTER listing the substance as GRAS in part 182, part 184, or part 186 of this chapter, as appropriate.

(c) A FEDERAL REGISTER notice determining that a substance is a food additive shall provide for the use of the additive in food or food contact surfaces as follows:

(1) It may promulgate a food additive regulation governing use of the additive.

(2) It may promulgate an interim food additive regulation governing use of the additive.

(3) It may require discontinuation of the use of the additive.

(4) It may adopt any combination of the above three approaches for different uses or levels of use of the additive.

(d) If the Commissioner of Food and Drugs is aware of any prior sanction for use of the substance, he will concurrently propose a separate regulation covering such use of the ingredient under part 181 of this chapter. If the Commissioner is unaware of any such applicable prior sanction, the proposed regulation will so state and will require any person who intends to assert or rely on such sanction to submit proof of its existence. Any regulation promulgated pursuant to this section constitutes a determination that excluded uses would result in adulteration of the food in violation of section 402 of the Act, and the failure of any person to come forward with proof of such an applicable prior sanction in response to the proposal will constitute a waiver of the right to assert or rely on such sanction at any later time. The notice will also constitute a proposal to establish a regulation under part 181 of this chapter, incorporating the same provisions, in the event that such a regulation is determined to be appropriate as a result of submission of proof

of such an applicable prior sanction in response to the proposal.

[42 FR 14488, Mar. 15, 1977, as amended at 42 FR 15673, Mar. 22, 1977; 54 FR 24896, June 12, 1989]

§ 170.39 Threshold of regulation for substances used in food-contact articles.

(a) A substance used in a food-contact article (e.g., food-packaging or food-processing equipment) that migrates, or that may be expected to migrate, into food will be exempted from regulation as a food additive because it becomes a component of food at levels that are below the threshold of regulation if:

(1) The substance has not been shown to be a carcinogen in humans or animals, and there is no reason, based on the chemical structure of the substance, to suspect that the substance is a carcinogen. The substance must also not contain a carcinogenic impurity or, if it does, must not contain a carcinogenic impurity with a TD₅₀ value based on chronic feeding studies reported in the scientific literature or otherwise available to the Food and Drug Administration of less than 6.25 milligrams per kilogram bodyweight per day (The TD₅₀, for the purposes of this section, is the feeding dose that causes cancer in 50 percent of the test animals when corrected for tumors found in control animals. If more than one TD₅₀ value has been reported in the scientific literature for a substance, the Food and Drug Administration will use the lowest appropriate TD₅₀ value in its review.);

(2) The substance presents no other health or safety concerns because:

(i) The use in question has been shown to result in or may be expected to result in dietary concentrations at or below 0.5 parts per billion, corresponding to dietary exposure levels at or below 1.5 micrograms/person/day (based on a diet of 1,500 grams of solid food and 1,500 grams of liquid food per person per day); or

(ii) The substance is currently regulated for direct addition into food, and the dietary exposure to the substance resulting from the proposed use is at or below 1 percent of the acceptable daily intake as determined by safety data in

the Food and Drug Administration's files or from other appropriate sources;

(3) The substance has no technical effect in or on the food to which it migrates; and

(4) The substance use has no significant adverse impact on the environment.

(b) Notwithstanding paragraph (a) of this section, the Food and Drug Administration reserves the right to decline to grant an exemption in those cases in which available information establishes that the proposed use may pose a public health risk. The reasons for the agency's decision to decline to grant an exemption will be explained in the Food and Drug Administration's response to the requestor.

(c) A request for the Food and Drug Administration to exempt a use of a substance from regulation as a food additive shall include three copies of the following information (If part of the submitted material is in a foreign language, it must be accompanied by an English translation verified to be complete and accurate in accordance with § 10.20(c)(2) of this chapter):

(1) The chemical composition of the substance for which the request is made, including, whenever possible, the name of the chemical in accordance with current Chemical Abstract Service (CAS) nomenclature guidelines and a CAS registry number, if available;

(2) Detailed information on the conditions of use of the substance (e.g., temperature, type of food with which the substance will come into contact, the duration of the contact, and whether the food-contact article will be for repeated or single use applications);

(3) A clear statement as to whether the request for exemption from regulation as a food additive is based on the fact that the use of the substance in the food-contact article results in a dietary concentration at or below 0.5 parts per billion, or on the fact that it involves the use of a regulated direct food additive for which the dietary exposure is at or below 1 percent of the acceptable dietary intake (ADI);

(4) Data that will enable the Food and Drug Administration to estimate the daily dietary concentration resulting from the proposed use of the sub-

stance. These data should be in the form of:

(i) Validated migration data obtained under worst-case (time/temperature) intended use conditions utilizing appropriate food simulating solvents;

(ii) Information on the amount of the substance used in the manufacture of the food-contact article; or

(iii) Information on the residual level of the substance in the food-contact article. For repeat-use articles, an estimate of the amount of food that contacts a specific unit of surface area over the lifetime of the article should also be provided. (In cases where data are provided only in the form of manufacturing use levels or residual levels of the substance present in the food-contact article, the Food and Drug Administration will calculate a worst-case dietary concentration level assuming 100 percent migration.) A detailed description of the analytical method used to quantify the substance should also be submitted along with data used to validate the detection limit.

(iv) In cases where there is no detectable migration into food or food simulants, or when no residual level of a substance is detected in the food-contact article by a suitable analytical method, the Food and Drug Administration will, for the purposes of estimating the dietary concentration, consider the validated detection limit of the method used to analyze for the substance.

(5) The results of an analysis of existing toxicological information on the substance and its impurities. This information on the substance is needed to show whether an animal carcinogen bioassay has been carried out, or whether there is some other basis for suspecting that the substance is a carcinogen or potent toxin. This type of information on the impurities is needed to show whether any of them are carcinogenic, and, if carcinogenic, whether their TD50 values are greater than 6.25 milligrams per kilogram bodyweight per day in accordance with paragraph (a)(1) of this section.

(6) Information on the environmental impact that would result from the proposed use of the substance. Depending on the type of use, this information

should be in the form of an abbreviated environmental assessment as specified in §25.31a(b)(1) or (b)(2) of this chapter.

(d) Data to be reviewed under this section shall be submitted to the Food and Drug Administration's Office of Premarket Approval (HFS-200), 200 C St. SW., Washington, DC 20204.

(e) The Food and Drug Administration will inform the requestor by letter whether the specific food-contact application is exempt from regulation as a food additive or not. Although a substance that migrates to food at a level that results in a dietary concentration at or below the threshold of regulation will not be the subject of a regulation published in the FEDERAL REGISTER and will not appear in the Code of Federal Regulations, the Food and Drug Administration will maintain a list of substances exempted from regulation as food additives under this section on display at the Dockets Management Branch. This list will include the name of the company that made the request, the chemical name of the substance, the specific use for which it has received an exemption from regulation as a food additive, and any appropriate limitations on its use. The list will not include any trade names. This list will enable interested persons to see the types of uses of food-contact materials being exempted under the regulation. Interested persons may also obtain a copy of the list of exempted substances by contacting the Food and Drug Administration's Office of Premarket Approval (HFS-200), 200 C St. SW., Washington, DC 20204. The agency's finding of no significant impact and the evidence supporting that finding, contained in an environmental assessment, also will be available for public inspection at the Dockets Management Branch in accordance with §25.41(b)(2) of this chapter. Requests for copies of releasable information contained in submissions requesting exemptions from the food additive regulations will be handled in accordance with the Food and Drug Administration's Freedom of Information Act procedures, as described in part 20 of this chapter. In particular, data and information that fall within the definitions of a trade secret or confidential commercial or financial information are not available

for public disclosure in accordance with §20.61(c) of this chapter.

(f) If the request for an exemption from regulation as a food additive is not granted, the requestor may submit a petition to the Food and Drug Administration for reconsideration of the decision in accordance with the provisions of §10.33 of this chapter.

(g) If the Food and Drug Administration receives significant new information that raises questions about the dietary concentration or the safety of a substance that the agency has exempted from regulation, the Food and Drug Administration may reevaluate the substance. If the Food and Drug Administration tentatively concludes that the information that is available about the substance no longer supports an exemption for the use of the food-contact material from the food additive regulations, the agency will notify any persons that requested an exemption for the substance of its tentative decision. The requestors will be given an opportunity to show why the use of the substance should not be regulated under the food additive provisions of the act. If the requestors fail to adequately respond to the new evidence, the agency will notify them that further use of the substance in question for the particular use will require a food additive regulation. This notification will be placed on public display at the Dockets Management Branch as part of the file of uses of substances exempted from regulation as food additives. The Food and Drug Administration recognizes that manufacturers other than those that actually made a request for exemption may also be using exempted substances in food-contact articles under conditions of use (e.g., use levels, temperature, type of food contacted, etc.) that are similar to those for which the exemption was issued. Because only requestors will be notified as part of the revocation process described in this section, the Food and Drug Administration plans to notify other manufacturers by means of a notice published in the FEDERAL REGISTER of its decision to revoke an exemption issued for a specific use of a substance in a food contact article.

(h) Guidelines to assist requestors in the preparation of submissions seeking

exemptions from the food additive regulations are available from the Food and Drug Administration's Office of Premarket Approval (HFS-200), 200 C St. SW., Washington, DC 20204. Interested persons are encouraged to obtain specific guidance from the Food and Drug Administration on the appropriate protocols to be used for obtaining migration data, on the validation of the analytical methods used to quantify migration levels, on the procedures used to relate migration data to dietary exposures, and on any other issue not specifically covered in the Food and Drug Administration's guidelines.

[60 FR 36595, July 17, 1995]

Subpart C—Specific Administrative Rulings and Decisions

§ 170.45 Fluorine-containing compounds.

The Commissioner of Food and Drugs has concluded that it is in the interest of the public health to limit the addition of fluorine compounds to foods (a) to that resulting from the fluoridation of public water supplies as stated in § 250.203 of this chapter, (b) to that resulting from the fluoridation of bottled water within the limitation established in § 103.35(d) of this chapter, and (c) to that authorized by regulations (40 CFR part 180) under section 408 of the Act.

§ 170.50 Glycine (aminoacetic acid) in food for human consumption.

(a) Heretofore, the Food and Drug Administration has expressed the opinion in trade correspondence that glycine is generally recognized as safe for certain technical effects in human food when used in accordance with good manufacturing practice; however:

(1) Reports in scientific literature indicate that adverse effects were found in cases where high levels of glycine were administered in diets of experimental animals.

(2) Current usage information indicates that the daily dietary intake of glycine by humans may be substantially increasing due to changing use patterns in food technology.

Therefore, the Food and Drug Administration no longer regards glycine and

its salts as generally recognized as safe for use in human food and all outstanding letters expressing sanction for such use are rescinded.

(b) The Commissioner of Food and Drugs concludes that by May 8, 1971, manufacturers:

(1) Shall reformulate food products for human use to eliminate added glycine and its salts; or

(2) Shall bring such products into compliance with an authorizing food additive regulation. A food additive petition supported by toxicity data is required to show that any proposed level of glycine or its salts added to foods for human consumption will be safe.

(c) The status of glycine as generally recognized as safe for use in animal feed, as prescribed in § 582.5049 of this chapter, remains unchanged because the additive is considered an essential nutrient in certain animal feeds and is safe for such use under conditions of good feeding practice.

§ 170.60 Nitrites and/or nitrates in curing premixes.

(a) Nitrites and/or nitrates are food additives when combined in curing premixes with spices and/or other flavoring or seasoning ingredients that contain or constitute a source of secondary or tertiary amines, including but not limited to essential oils, disodium inosinate, disodium guanylate, hydrolysates of animal or plant origin (such as hydrolyzed vegetable protein), oleoresins of spices, soy products, and spice extractives. Such food additives may be used only after the establishment of an authorizing food additive regulation. A food additive petition submitted pursuant to §§ 171.1 and 171.100 of this chapter, supported by data demonstrating that nitrosamines are not formed in curing premixes containing such food additives, is required to establish safety.

(b) Nitrites and/or nitrates, when packaged separately from flavoring and seasoning in curing premixes, may continue to be used under prior sanctions in the commercial curing of meat and meat products and poultry products and in accordance with the provisions of §§ 172.170 and 172.175 of this chapter that apply to meat curing preparations for the home curing of